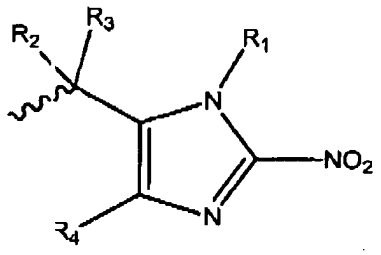
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-52. (Canceled)

53. (Previously Presented) A protected anti-neoplastic agent, in which the anti-neoplastic agent is an alkylating agent, and includes one or more protectable hydroxyl groups or amine groups, and wherein one or more of the protectable hydroxyl groups or amine groups is substituted with a group selected from Hyp-L- or Hyp-, wherein Hyp is a hypoxic activator having the formula



wherein R_1 is substituted or unsubstituted C_1-C_6 alkyl or substituted or unsubstituted C_1-C_6 alkoxy;

R_2 is hydrogen;

R_3 is -H or C_1-C_6 alkyl; and

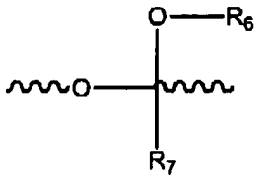
R_4 is -H, substituted or unsubstituted C_1-C_6 alkyl, or substituted or unsubstituted C_1-C_6 alkoxy;

wherein the R_1 and R_4 substituted alkyl and substituted alkoxy are independently substituted with one or more heteroatom-containing groups selected from ether (-OR^{20}), amino (-NH_2), mono-substituted amino (-$NR^{20}H$), di-substituted amino (-$NR^{21}R^{22}$), cyclic C_1-$_5$ alkylamino, imidazolyl, C_1-$_6$ alkylpiperazinyl, morpholino, thiol (-SH), thioether -(SR^{20}), tetrazole, carboxylic acid (-COOH), ester (-$COOR^{20}$), amide (-$CONH_2$), mono-substituted amide

(-CONHR^{20}), disubstituted amide (-CONR^{21}R^{22}), N-connected amide (-NH$_2$-C(=O)-R^{20}), mono-substituted N-connected amide (-NHR^{21}-C(=O)-R^{20}), disubstituted N-connected amide (-NR^{21}R^{22}-S(=O)$_2$-R^{20}), N-connected sulfonamide (-NH$_2$-S(=O)$_2$-R^{20}), mono-substituted N-connected sulfonamide (-NHR^{21}-S(=O)$_2$-R^{20}), disubstituted N-connected sulfonamide (-NR^{21}R^{22}-S(=O)$_2$-R^{20}), sulphoxy (-S(=O)$_2$OH), sulphonate (S(=O)$_2$OR^{20}), sulphonyl (S(=O)$_2$R^{20}), sulphixy (S(=O)OH), sulphinate (S(=O)OR^{20}), sulphinyl (S(=O)R^{20}), phosphonooxy (OP(=O)(OH)$_2$), phosphate (OP(=O)(OR^{20})$_2$), and sulfonamide (-S(=O)$_2$NH$_2$, -S(=O)$_2$NHR^{21}, or -S(=O)$_2$NR^{21}R^{22}), where R^{20}, R^{21}, and R^{22} are independently selected from a C$_1$-C$_6$ alkyl group; and

L is a linking group of the formula ~~X——Y~~ , where X is selected from

and



wherein R$_6$ is unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups;

R$_7$ is hydrogen, unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups; and

Y is a spacer group selected from a substituted or unsubstituted -(CH$_2$)$_n$- chain with n=1-4; a substituted or unsubstituted -(CH$_2$)$_n$- chain with n=1-4 in which one of the carbon backbone chain atoms is substituted by a heteroatom containing group; or a delayed release group comprising an aromatic group.

54. (Canceled)

55. (Previously Presented) The protected anti-neoplastic agent of claim 53, wherein

R6 is unsubstituted C1-C3 alkyl or C1-C3 alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide,

sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano;

R7 is hydrogen, unsubstituted C1-C3 alkyl, or C1-C3 alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; and

the spacer group Y is an unsubstituted $-(CH_2)_n-$ chain with n=1-4, or a $-(CH_2)_n-$ chain with n=1-4 substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; or

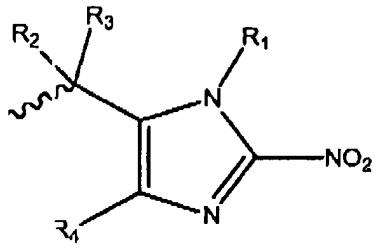
the spacer group Y is the delayed release group and has the formula $\sim\sim R_{10}—R_{11}—R_{12}\sim\sim$ where R10 is a bond; R11 is an unsubstituted or substituted aryl or substituted or unsubstituted heteroaryl group; and R12 has the formula $-(CR^{40}R^{41})-R^{42}-$ or $-(CR^{40}R^{41})-CR^{43}=CR^{44}-R^{42}-$, where R^{42} is a bond or -OC(=O)-, and R^{40}, R^{41}, R^{42}, and R^{43} are independently selected from -H, unsubstituted C_1-C_{10} alkyl, and C_1-C_{10} alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide, aldehydo, keto, amino, halo, and cyano.

56-87. (Canceled)

88. (Previously Presented) A method for treating cancer comprising administering to a subject a therapeutically effective amount of a protected anti-neoplastic agent according to claim 53, wherein the cancer is selected from the group consisting of colon cancer, prostate cancer, lung cancer, non-small cell lung cancer, liver cancer, skin cancer, sarcomas, pancreatic cancer, breast cancer, head and neck cancer, and myeloma.

89. (Previously Presented) A protected anti-neoplastic agent of formula Hyp-L-N or Hyp-N,

wherein Hyp is a hypoxic activator moiety of formula



wherein R_1 is unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups;

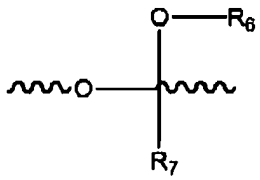
R_2 is hydrogen;

R_3 is hydrogen or C_1-C_6 alkyl; and

R_4 is hydrogen, unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups;

L is a linking group of the formula 

, wherein X is selected from

or


wherein R_6 is unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups;

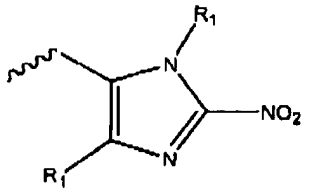
R_7 is hydrogen, unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups; and

Y is a spacer group selected from a substituted or unsubstituted $-(CH_2)_n-$ chain with n=1-4; a substituted or unsubstituted $-(CH_2)_p$-HAC-$(CH_2)_q-$ chain wherein each p and q

independently is 1 - 3 and p + q is less than or equal to 3 and HAC is a heteroatom containing group; and a delayed release group comprising an aromatic group; and

N is an anti-neoplastic alkylating agent.

90. (Previously Presented) The protected anti-neoplastic agent of claim 89 wherein Hyp is of the formula

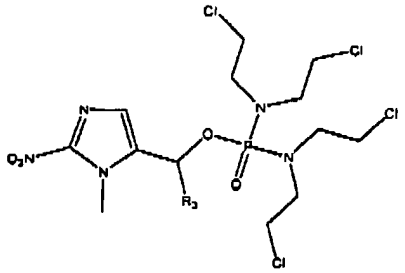


wherein R_1 and R_4 are each independently hydrogen or alkyl selected from methyl, ethyl, n-propyl, n-butyl, n-pentyl, t-butyl, cyclohexyl, cyclopentyl, and isopropyl, wherein the alkyl is optionally substituted with one or more heteroatom-containing groups; with the proviso that R_1 is not hydrogen.

91. (Canceled)

92. (Currently Amended) The protected anti-neoplastic agent of claim 90 wherein the alkylating agent is selected from the group consisting of cyclophosphamide, ifosfamide, melphalan, chlorambucil, thiotepa~~, and analogs thereof~~.

93. (Previously Presented) The protected anti-neoplastic agent of claim 89 of formula



wherein R_3 is hydrogen or C_1-C_6 alkyl.

94-98. (Canceled)

99. (Currently Amended) The protected anti-neoplastic agent of claim 55, wherein the alkylating agent is selected from the group consisting of cyclophosphamide, ifosfamide, melphalan, chlorambucil, thiotepa~~, and analogs thereof~~.

100. (Canceled)

101. (New) The protected anti-neoplastic agent of claim 53, wherein the one or more protectable hydroxyl groups or amine groups is substituted with Hyp-.

102. (New) The protected anti-neoplastic agent of claim 53, wherein only one of the one or more protectable hydroxyl groups or amine groups is substituted with Hyp- or Hyp-L-.

103. (New) The protected anti-neoplastic agent of claim 102, wherein the one protectable hydroxyl group or one protectable amine group is substituted with Hyp-.

104. (New) The protected anti-neoplastic agent of claim 103, wherein a hydroxyl group is substituted with Hyp-.

105. (New) The method of claim 88, wherein the one or more protectable hydroxyl groups or amine groups of the anti-neoplastic agent is substituted with Hyp-.

106. (New) The method of claim 88, wherein only one of the one or more protectable hydroxyl groups or amine groups is substituted with Hyp- or Hyp-L-.

107. (New) The method of claim 106, wherein the one protectable hydroxyl group or one protectable amine group is substituted with Hyp-.

108. (New) The protected anti-neoplastic agent of claim 107, wherein a hydroxyl group is substituted with Hyp-.

109. (New) The protected anti-neoplastic agent of claim 89 of formula Hyp-N.

110. (New) The protected anti-neoplastic agent of claim 90 of formula Hyp-N.